2) Information Disclosure Statement

The Office Action states that the Information Disclosure Statement filed May 6, 2005 fails to comply with 37 C.F.R. § 1.98(a)(2). Applicants hereby submit an IDS including a copy of each of foreign patent document.

3) Rejection of Claims 1-11 Under 35 U.S.C. 103

Claims 1-10 stand rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over Chen et al. (US 2002/0032171, "Chen"); and claims 1-7 and 9-11 under 35 U.S.C. 103(a), over Lambert et al. (US 6,458,373, "Lambert"). Applicants respectfully traverse the rejections for the reasons provided below.

A. The present invention

The present invention recited in presently pending claims 1-8 is directed to a method for preparing a microemulsion concentrate for oral administration of a water-insoluble anti-cold drug comprising (a) dissolving the water-insoluble anti-cold drug in a co-surfactant (e.g, "ethanol") to obtain a homogeneous drug solution; (b) adding a surfactant and an oil in the drug solution to obtain a microemulsion pre-concentrate; and (c) removing the co-surfactant from the pre-concentrate and claims 9-11 are related to a microemulsion concentrate prepared by the method.

The microemulsion concentrate of the present invention provides markedly improved bioavailability of the water-insoluble anti-cold drug when orally administered, and such drug

bioavailability is little influenced by pH change, thereby significantly decreasing the influences of the ingested food and individual absorption difference.

B. Summary of cited references

By way of review, Chen discloses a pharmaceutical composition comprising: (a) a carrier comprising a triglyceride and at least two surfactants, at least one of the surfactants being hydrophilic; and (b) a therapeutically effective amount of a polysaccharide drug, wherein the triglyceride and surfactants are present in amounts such that upon mixing with an aqueous medium in an aqueous medium to carrier ratio of about 100:1 by weight, the carrier forms a clear aqueous dispersion having an absorbance of less than about 0.3 at 400nm (see claim 1). Chen also teaches that the pharmaceutical composition can optionally include "solubilizers" to enhance the solubility of the therapeutic agent or the triglyceride in the composition, wherein "ethanol" is exemplified as one of the solubilizers (see paragraphs [0164] to [0166]).

Lambert discloses a pharmaceutical composition comprising a chemotherapeutic agent which is a taxoid, a taxane or a taxine; a tocopherol; tocopherol polyethylene glycol succinate (TPGS); polyethylene glycol; a surfactant; and an aqueous phase, wherein the composition is an emulsion or a microemulsion having an oil phase and a water phase, and all of the therapeutic agent is in the oil phase (see claim 1). Furthermore, in Example 4 of Lambert, it is disclosed that an emulsion form of the pharmaceutical composition was prepared by a process which comprises the steps of dissolving in an "ethanol" solvent the chemotherapeutic agent (i.e., paclitaxel), tocopherol, the surfactant (i.e., ascorbyl 6-palmitate) and TPGS, and then removing the ethanol solvent in vacuum.

C Comparison of the present invention with the cited references

As described above, the feature of the inventive method, which comprises first dissolving the water-insoluble anti-cold drug in the co-surfactant such as "ethanol" and then adding the surfactant and oil thereto, followed by removal of the co-surfactant therefrom, resides in mixing specific components in a specific order prior to the removal of the co-surfactant.

Specifically, when the water-insoluble anti-cold drug alone is dissolved in the co-surfactant having high solubility thereto, the drug solution thus obtained includes the drug in a very stable state. Subsequently, the addition of two components, the surfactant and oil, to the drug solution generates a microemulsion concentrate containing very stable emulsified drug microparticles after the removal of the co-surfactant. The emulsified drug microparticles contained in the inventive microemulsion concentrate are so stable toward the pH change that the change of its emulsified state causing the precipitation of the drug never occurs.

The inventive microemulsion concentrate may easily form microparticles having an average particle size ranging from about 270 to 500nm upon contact with an aqueous solution. Accordingly, the inventive microemulsion concentrate can provide a remarkably improved bioavailability of the drug when orally administered, which is little influenced by pH change (see lines 7-17, page 7 of the present specification). Such beneficial effects of the present invention are fully supported by Test Examples 1 (dissolution test), 2 (analysis of the emulsified drug microparticles), 3 (precipitation formation test) and 4 (absorption test) of the specification as originally filed.

In contrast, as shown above, although Chen and Lambert disclose the use of "ethanol" as a solvent or solubilizer in preparing the pharmaceutical composition, both are silent on the above-mentioned feature of the inventive method.

As a matter of fact, in Example 4 of the Lambert patent, the preparation of the pharmaceutical composition was performed by concurrent mixing of the active ingredient, tocopherol, the surfactant, TPGS and ethanol, followed by removing ethanol. In such a process, it is expected that the surfactant and the oil undesirably act as "anti-solvents" against the active ingredient due to their lower solubilizing ability as compared to that of ethanol, which results in crystallization and/or precipitation of the active ingredient in the formed microemulsion pre-concentrate, as well as low emulsion stability of the formed final microemulsion concentrate, leading to reduced bioavailability of the active ingredient.

To further illustrate and demonstrate the benefit achievable by the present invention, the applicant submits a declaration in accordance with 37 C.F.R. section 1.132 together with this response. This declaration shows the results of comparative experiments carried out with the inventive microemulsion pre-concentrate (as an intermediate product) of Example 1 and comparative microemulsion pre-concentrates obtained by simultaneously mixing all components, which illustrate that the inventive microemulsion pre-concentrates are clearly superior over the comparative microemulsion pre-concentrates in terms of the solubility and dissolution rate of the active ingredient, and the emulsion stability.

As described above, it is believed that the methods disclosed in the present invention and cited references are obviously different, and the unique feature of the present invention as well as

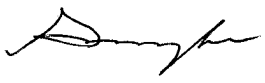
the beneficial effects arising therefrom are not taught, suggested or implied by the cited references, even if they are combined.

Accordingly, the present invention of claims 1-11 is clearly patentable and would not have been obvious to one skilled in the art over the cited references, and it is respectfully submitted that the 103 rejections of claims 1-11 be withdrawn.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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Date: February 12, 2007

ATTACHMENT: Declaration Under 37 C.F.R. § 1.132